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SUPPLEMENT ARTICLE

WILEY CLINICAL ORAL IMPLANTS RESEARCH

The use of platelet-rich plasma to enhance the outcomes of implant therapy: A systematic review

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Abstract

Objective: To assess the effect of platelet-rich plasma (PRP) on implant dentistry. The primary focused question was as follows: What are the clinical, histological, and radiographic outcomes of PRP administration for bone regeneration and implant therapy?

Methods: A literature search was conducted involving three databases: MEDLINE, EMBASE and Cochrane database followed by a hand search of relevant scientific journals. Human studies using PRP for bone regeneration and implant therapy were considered and articles published up to December 31, 2017 were included. Eligible studies were selected based on the inclusion criteria, and quality assessments were conducted.

Results: In total, out from the 9,497 titles meeting the original search criteria, 22 fulfilled the inclusion criteria and were chosen for data extraction. Among them were 15 randomized controlled trials (RCT) and seven controlled clinical trials (CCT). Overall, the risk of bias was moderate to high. A total of seven studies showed superior outcomes when PRP was added during sinus floor elevation and five showed no superior outcome. Three studies found a significant advantage of PRP for alveolar bone regeneration and another three studies for soft tissue healing. Three studies reported on beneficial effects of PRP directly during implant placement while another study failed to find significant differences. Due to the heterogeneity of study designs, no meta-analysis could be performed.

Summary and Conclusions: Despite the lack of consistent evidence supporting the clinical benefit of PRP in healthy patients, PRP might have a positive effect on wound healing and bone regeneration in compromised patients.

KEYWORDS

alveolar ridge preservation, bone regeneration, implant therapy, platelet-rich plasma, sinus floor elevation

1 | INTRODUCTION

Implant therapy is considered a predictable treatment with excellent long-term results. When teeth are lost, the alveolar process undergoes dimensional changes (Schropp, Wenzel, Kostopoulos, & Karring, 2003). The magnitude of these dimensional changes is clinically relevant for a comprehensive treatment planning. Furthermore, traumatic tooth loss during growth, multiple or longlasting edentulism, extensive bone and soft tissue resorption can hinder implant placement. Consequently, implant placement is often combined with augmentative procedures

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such as alveolar ridge preservation, guided bone regeneration, or sinus floor elevation (SFE) for an ideal prosthetic position of the implant.

Platelets play a fundamental role in the early stages of wound healing and bone regeneration by releasing growth factors and other molecules (Singer & Clark, 1999). Among the growth factors are platelet-derived growth factor, transforming growth factor-beta, but also cytokines, chemokines, and other molecules together targeting the various cell types involved in early wound healing and bone regeneration (Klinger & Jelkmann, 2002; Nurden, 2011). Activated platelets form aggregates with the fibrin-rich matrix as part of the hemostasis and thrombosis (Singer & Clark, 1999). One therapeutic concept is based on the assumption that if physiologic concentrations of activated platelets are good, a supra-physiological concentration of activated platelets even better support the early stages of wound healing and bone regeneration.

Platelet-rich plasma (PRP) and platelet concentrate reached the field of dentistry in the 90s (Marx et al., 1998). Since then, slightly different protocols for preparing PRP have been established. In general, anticoagulated blood is subjected to a first "soft" spin to separate the plasma fraction from the erythrocytes. The plasma fraction is subjected to a second "hard" spin to separate the platelets from the platelet poor plasma (PPP). The platelet-pellet containing leukocytes is suspended in a lower volume of PPP and activated by thrombin and calcium. Through this dual centrifugation process, platelets are around 2 to 5-fold enriched compared to normal blood (Oudelaar, Peerbooms, Huis In 't Veld, & Vochteloo, 2018).

In recent years, systematic reviews have gathered evidence on the clinical impact of PRP on SFE (Lemos et al., 2016; Pocaterra et al., 2016), alveolar ridge preservation (Del Fabbro, Corbella, Taschieri, Francetti, & Weinstein, 2014; Moraschini & Barboza, 2015) and periodontal intrabony defects (Hou, Yuan, Aisaiti, Liu, & Zhao, 2016). The present systematic review is an update of the evidence for the use of PRP in implant therapy. It covers all aspects of implant therapy, from pre-implantation measures to augmentative procedures and observations during the healing phase.

2 | MATERIAL AND METHODS

2.1 | Protocol development and eligibility criteria

This review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement, conforming to which a detailed protocol was established (Liberati et al., 2009; Moher et al., 2015).

The focused question was formulated based on the PRISMA guidelines.

1. Population (P) = humans with lack of alveolar bone and/or need of implant therapy or tooth extraction.
2. Intervention (I) = use of PRP alone or in combination with a graft material in guided bone regeneration techniques and implant therapy.
3. Comparison (C) = respective surgical procedure without PRP.
4. Outcome (O) = alveolar bone regeneration, soft tissue healing, graft resorption, osseointegration, implant stability and postoperative life quality issues such as pain and swelling.
5. Study design (S) = randomized, controlled clinical trials (CCTs), prospective CCTs, split-mouth or parallel arms.

The following PICOS question was raised: Is there any additional benefit of PRP on guided bone regeneration and implant therapy over traditional approaches in terms of clinical, histological and radiographic outcomes?

2.2 | Search strategy

An electronic search of three databases (MEDLINE, EMBASE, CENTRAL) was performed. Articles published up to December 31, 2017 were considered. No language or time restrictions were applied in the search. However, only studies written in English were included for selection. An additional hand search was carried out encompassing the bibliographies of the included papers and other narrative and systematic reviews as well as in the following journals: *Clinical Oral Implants Research*, *Clinical Implant Dentistry and Related Research*, *European Journal of Oral Implantology*, *Implant Dentistry*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Periodontics and Restorative Dentistry*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Clinical Oral Investigations*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Periodontology*, *Oral Surgery*, *Oral Medicine*, *Oral Radiology*, *Oral Pathology and Endodontics*.

2.3 | Search terms

The electronic search strategy included terms related to the intervention and used the following combination of key words, MeSH and Emtree terms: "osseointegration" OR "dental implants, single-tooth" OR "dental implants" OR "tooth implant" OR "guided bone regeneration" OR "bone regeneration" OR "alveolar ridge augmentation" OR "alveolar bone loss" OR "bone resorption" OR "tooth extraction" OR "socket preservation" OR "alveolar process" OR "alveolar ridge preservation" OR "sinus floor augmentation" OR "sinus lifting" OR "sinus lift" OR "maxillary sinus" AND "platelets" OR "platelet-rich plasma" OR "PRP" OR "leukocyte platelet plasma" OR "pure platelet-rich plasma "OR "P-PRP "OR "LPRP "OR "L-PRP "OR "advanced platelet-rich plasma" OR "platelet gel" OR "autogenous cells" OR "advanced PRP" OR "A-PRP" OR "APRP" OR "LPRP gel" OR "leukocyte and platelet-rich plasma gel" OR "plasma rich in growth factors". Cochrane search filters for randomized controlled trials (RCTs) and CCTs were implemented, with cohort trials also included. The results were limited to human studies.

2.4 | Inclusion criteria

1. RCTs or CCTs including at least 10 patients/sites per group.
2. Studies regarding SFE, alveolar ridge preservation, bone augmentation procedures, soft tissue healing or implant therapy combined with PRP.

2.5 | Exclusion criteria

In vitro and preclinical studies, cohort studies, case series, case reports, retrospective studies and RCT or CCT with less than 10 patients/sites per group and studies not meeting all inclusion criteria.

2.6 | Screening and selection of studies

Publication records and titles identified by the electronic search and hand search were independently screened by two reviewers (FJS and AS), based on the inclusion criteria. No restrictions were applied neither for languages, years considered nor for publication status. Discrepancies were solved by discussion including a third reviewer (RG). Cohen's Kappa-coefficient was used as a measure of agreement between the readers. Thereafter, full texts of the selected abstracts were obtained. Where full texts could not be obtained authors and editors of the respective journal were contacted. The two reviewers independently performed the whole screening process, i.e., from the MeSH and Emtree term search up to the full-text examination. Then, articles that met the inclusion criteria were processed for data extraction.

2.7 | Data extraction and quality assessment

The inclusion criteria were applied for data extraction. The studies were classified according to study design and type of intervention. Then, outcomes were compiled in tables. All extracted data were double-checked, and any questions that came up during the screening and the data extraction were discussed within the authors to aim for consensus. Two reviewers (FJS and AS) independently evaluated the methodological quality of all included studies using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials (Higgins et al., 2011). All included studies were checked for the following criteria: (a) sequence generation (b) allocation concealment (c) blinding of participants and personnel (d) blinding of outcome assessment (e) incomplete outcome data (f) selective reporting (g) other bias. Any disagreement was discussed until consensus was achieved. Each study was classified into the following groups: low risk of bias if all quality criteria were judged as "present", moderate risk of bias if one or more key domains were "unclear", and high risk of bias if one or more key domains were not "present".

3 | RESULTS

3.1 | Selection of studies

The literature search identified 8,975 potential references in Medline and 517 in Embase of which 54 were eligible after title and abstract screening (inter-reviewer agreement $\kappa = 0.914 \pm 0.059$). Hand search identified five more studies (Anitua, Murias-Freijo, Alkhraisat, & Orive, 2015; Dugrillon, Eichler, Kern, & Kluter, 2002; Geurs et al., 2014; Mozzati, Gallesio, di Romana, Bergamasco, & Pol, 2014; Raghoebar et al., 2005). Of the 59 full-text articles, 27 did not meet the inclusion criteria and were excluded (Figure 1; Table 1 of excluded studies). The remaining 18 RCTs and 14 CCTs were discussed in the EAO consensus meeting. Studies dealing with third molar extractions were excluded (Table 1). Consequently, 15 RCTs and seven CCTs were included for data extraction. The included studies were divided into subgroups, depending on the area of PRP application (Tables 2–4):

1. SFE (Table 2): *n* = 12 (Bettega et al., 2009; Cabbar, Guler, Kurkcu, Iseri, & Sencift, 2011; Consolo, Zaffe, Bertoldi, & Ceccherelli, 2007; Del Fabbro, Corbella, Ceresoli, Ceci, & Taschieri, 2015; Kumar, Shaik, Nadella, & Chintapalli, 2015; Schaaf, Streckbein, Lendeckel, Heidinger, Rehmann, et al., 2008; Schaaf, Streckbein, Lendeckel, Heidinger, Gortz, et al., 2008; Stenport, Ortorp, & Thor, 2011; Thor, Sennerby, Hirsch, & Rasmusson, 2007; Thor, Wannfors, Sennerby, & Rasmusson, 2005; Torres et al., 2009; Wiltfang et al., 2003).
2. Alveolar bone regeneration (Table 3a and 3b):
   (a) Alveolar ridge preservation (Table 3a) *n* = 4 (Alissa, Esposito, Horner, & Oliver, 2010; Anitua et al., 2015; Farina, Bressan, Taut, Cucchi, & Trombelli, 2013; Mozzati et al., 2014).
   (b) Alveolar ridge augmentation (Table 3b) *n* = 2 (Eskan et al., 2014; Torres et al., 2010).
3. Dental implants (Table 4): *n* = 4 (ArRejaie, Al-Harbi, Alagl, & Hassan, 2016; Georgakopoulos et al., 2014; Kundu & Rathee, 2014; Monov et al., 2005).

3.2 | Exclusion of studies

Exclusion of studies (Table 1) occurred due to: insufficient study cohort, missing control group, unavailability of full text, not PRP used and application during third molar extraction.

3.3 | Quality assessment of the included studies

Quality and risk assessment was independently conducted by two authors (FJS and AS) and are represented in Figures 2 and 3. Discrepancies were solved by discussion until reaching consensus. Included RCTs and CCTs were rated following the Cochrane collaboration's tool for assessing risk of bias. Two studies demonstrated low risk of bias for all but one criteria and the majority showed a moderate to high risk of bias. Most studies failed to provide a detailed report about both randomization and allocation concealment and other key domains increasing the risk of bias. Nine studies described the randomization process, 6 the allocation concealment in sufficient detail. One study was registered to an online database which allows for judgment of selective outcome bias. Adequate blinding of patients and personnel was stated in five trials, blinding of surgeons in four, and blinding of outcome assessors in

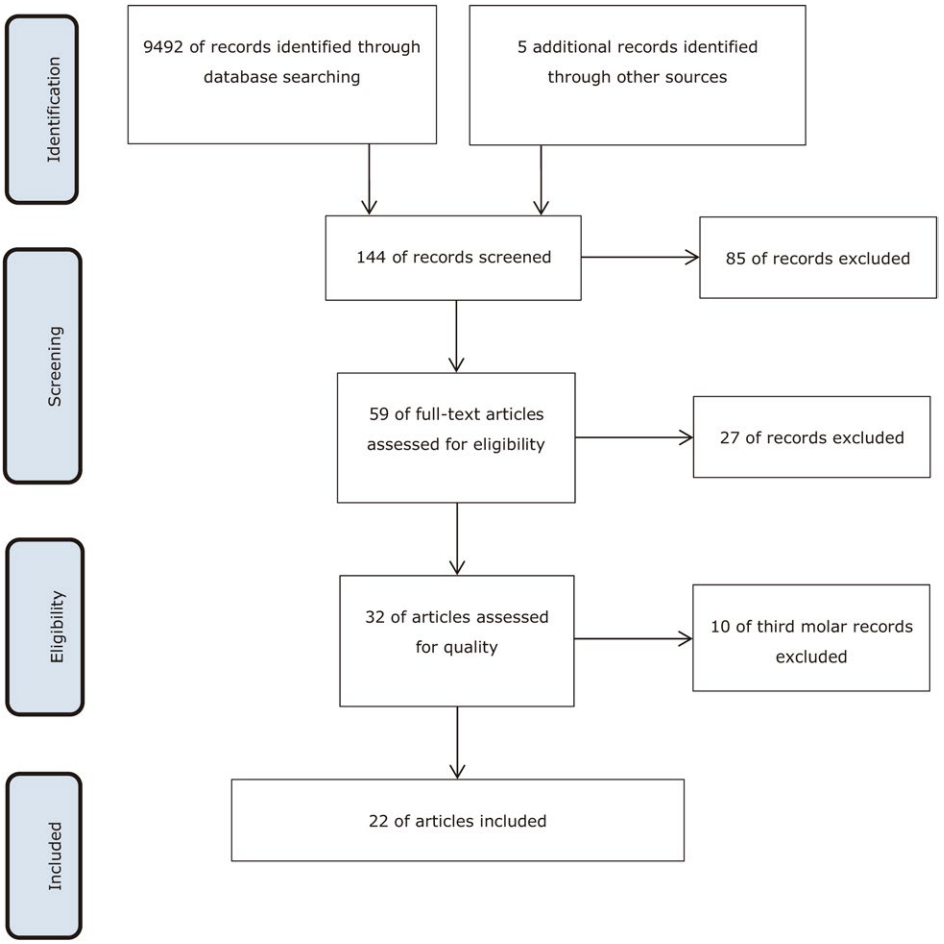

FIGURE 1 PRISMA flow diagram

nine trials. None of the studies provided an intention-to-treat analysis of their patients and only four studies described sample size calculations.

3.4 | Study design and evaluation period

Fifteen RCTs and seven CCTs were included. A total of six studies were RCTs where a split-mouth design was applied (ArRejaie et al., 2016; Bettega et al., 2009; Consolo et al., 2007; Mozzati et al., 2014; Schaaf, Streckbein, Lendeckel, Heidinger, Rehmann, et al., 2008; Torres et al., 2009) The remaining nine RCTs used a parallel group design. Of the CCTs, five were designed as split mouth (Cabbar et al., 2011; Monov et al., 2005; Stenport et al., 2011; Thor et al., 2005, 2007), two as parallel group studies (Farina et al., 2013; Kumar et al., 2015). The follow-up period ranged considerably from 10 days to 30 months.

3.5 | Subject characteristics

All but one study (Mozzati et al., 2014) included healthy subjects with no active inflammatory disease. The mean age varied from 18 to 80. The number of included patients lied between 10 and 80. Smokers were included in eight, excluded in seven and not reported in seven studies.

3.6 | Data extraction

Included studies presented a high heterogeneity in regards to outcome measures, PRP preparation or study duration. Therefore, a meta-analysis was not feasible.

3.7 | Sinus floor elevation (totally 374 patients)

All included studies (12) applied PRP in combination with iliac bone (seven), autologous intraoral bone grafts (one), β-tricalcium phosphate (β-TCP; one), bovine bone graft (BBG) (Unilab Surgibone®/one study) and deproteinized bovine bone mineral (DBBM, two). Table 2 depicts the outcome measures of included studies.

Iliac bone graft (Bettega et al., 2009; Consolo et al., 2007; Schaaf, Streckbein, Lendeckel, Heidinger, Rehmann, et al., 2008; Schaaf, Streckbein, Lendeckel, Heidinger, Gortz, et al., 2008; Stenport et al., 2011; Thor et al., 2005, 2007): no statistical differences in resonance frequency analysis values for the posterior maxilla, but significant differences for the anterior maxilla

TABLE 1 List of excluded full-text papers and reasons for exclusion following full-text screening

Author and year	Reasons for exclusion
Antonello et al. (2013)	Third molar extraction
Arenaz-Bua et al. (2010)	Third molar extraction
Barbu et al. (2016)	Not PRP
Badr et al. (2010)	Less than 10 patients per group
Célio-Mariano et al. (2011)	Third molar extraction
Cheah et al. (2014)	Less than 10 patients per group
Comert et al. (2017)	Less than 10 patients per group
Dasmah et al. (2013)	No control group
Dugrillon et al. (2002)	No control group
Dutta et al. (2015)	Third molar extraction
Dutta et al. (2016)	Third molar extraction
Garg et al. (2000)	No full text available, author so far not responding
Gawande et al. (2009)	Third molar extraction
Gelbart et al. (2005)	No control group
Geurs et al. (2014)	Less than 10 patients per group
Kassolis et al. (2005)	PRP being not the only variable
Kaul et al. (2012)	Third molar extraction
Khairy et al. (2013)	Less than 10 patients per group
Kilic et al. (2016)	Less than 10 patients per group
Kutkut et al. (2012)	PRP being not the only variable
Maiorana et al. (2003)	No control group
Malik et al. (2012)	No full text available, email of author expired
Matsuo et al. (2011)	11 samples taken from only 5 patients
Mazor et al. (2004)	No control group
Menezes et al. (2015)	PRP being not the only variable
Mozzati et al. (2010)	Third molar extraction
Ntounis et al. (2015)	Same study cohort as Geurs 2014
Ogundipe (2011)	Third molar extraction
Raghoebar et al. (2005)	Insufficient number of patients
Rutkowski et al. (2010)	Insufficient number of patients
Sammartino et al. (2003)	No control group
Simon et al. (2004)	No full text available, email of author expired
Steigmann et al. (2005)	PRP being not the only variable
Taschieri et al. (2012)	Insufficient number of patients
Varghese et al. (2017)	Not PRP
Vivek et al. (2009)	Third molar extraction
Wallace et al. (2010)	No control group

at abutment connection and at 1-year follow-up was reported by one study (Thor et al., 2005). Higher densitometric and trabecular bone values for time-periods up to 6 months were found in favor of PRP (Consolo et al., 2007). Thor and coworkers showed superiority of bone formation after 3 months for the PRP group, which disappeared after 6 months, yet biopsies were not obtained from all patients (Thor et al., 2007). No additive effects of PRP were found in survival rate (Thor et al., 2005), augmentation height (Bettega et al., 2009), marginal bone level changes (Thor et al., 2005), bone density (Bettega et al., 2009; Schaaf, Streckbein, Lendeckel, Heidinger, Rehmann, et al., 2008), volume of both lamellar and woven bone (Bettega et al., 2009), volume of new bone (Schaaf, Streckbein, Lendeckel, Heidinger, Gortz, et al., 2008) and angiogenesis (Stenport et al., 2011).

Autologous intraoral bone grafts: In terms of bone height after grafting significant differences were found immediately and 6 months after surgery (Kumar et al., 2015).

Bovine bone graft: there was only one study using BBG (Unilab Surgibone®) (Cabbar et al., 2011) and no additional effects of PRP were found when looking at implant survival rates, ISQ values, soft tissue healing, and histological parameters such as residual amount of graft, or trabecular bone structure.

Deproteinized bovine bone mineral: two studies combined DBBM with PRP. One study using DBBM demonstrated that PRP was associated with significantly less pain and higher quality of life parameters post-surgery (Del Fabbro et al., 2015). The other study using DBBM showed that PRP significantly increased new bone formation (Torres et al., 2009). However, histomorphometric analysis was only performed in five patients with a split-mouth design and the implant survival rate was not affected by PRP (Torres et al., 2009).

3.8 | Alveolar ridge preservation (totally 145 patients)

One study evaluated the use of PRP for ridge preservation. A denser trabecular pattern, less pain sensation and better soft tissue healing (Alissa et al., 2010) were reported. Three studies used PRGF (Anitua et al., 2015; Farina et al., 2013; Mozzati et al., 2014). Anitua et al. (2015) analyzed outcome measures such as regenerated socket volume, bone density, soft tissue healing, pain, and histomorphometric characteristics like keratinized gingival thickness and percentage of new bone formation. The results demonstrated that PRGF in mandibular molar extraction sites yielded superior results for all assessed outcomes. Superior results for PRGF were described in diabetic patients: less pain during the first 14 days and a smaller residual socket volume during the first 7 days were observed in the test group (Mozzati et al., 2014). However, no differences in terms of mineral density and mineralization were described by Farina (Farina et al., 2013) (Table 3a).

3.9 | Alveolar ridge augmentation (totally 62 patients)

Only two studies were found, both of which showed better results with PRP. Ridge width at the marginal crest was higher in the PRP group as well as the percentage of vital bone (Eskan et al., 2014). PRP further enhanced the average gain of bone height and width and

TABLE 2 Included studies: sinus floor elevation

Study (year), funding	Study design, duration	No. of patients (implants)	Mean age ± *SD* and/or range	Surgical procedure	Groups T: test C: control (Smokers included)	PRP preparation	Outcome
Bettega et al. (2009) Institutional	RCT split-mouth 6 months	18	50.5 ± NR 44–57	Bilateral SFE + iliac crest bone graft w/wo APC	T: PRP *n* = 16 C: no PRP *n* = 16 (No)	NR	*Sinus floor height augmentation (mm):* NS (T: 11.5 vs. C: 10.0, $p > 0.05$) *CT scan Hounsfield density:* NS (T: 331 vs. C: 342, $p > 0.05$) *Histology:* - total bone volume (%): NS (T: 40 vs. C: 50, $p > 0.05$) - lamellar and woven bone volume (%): NS (T: 37.1 vs. C: 42.5, $p > 0.05$)
Cabbar et al. (2011) NR	CCT split-mouth 12-14 months	10 (28)	53.7 ± 0.8 45–67	SFE + BBG w/wo PRP	T: BBG + PRP *n* = 14 C: BBG *n* = 14 (No)	2,400 rpm/10 min 3,600 rpm/15 min	*Implant success (%):* Overall success 92.8%, NS between the groups at 6 months (T: NR vs. C: NR, $p > 0.05$) *Histology:* - soft tissue (%): NS (T: 57.8 ± 4.4 vs. C: 59.9 ± 7.5, $p = 0.251$) - residual graft (%): NS (T: 23.6 ± 5.9 vs. C: 21.9–6.6, $p = 0.168$) - new bone (%): NS (T: 16.1 ± 3.8 vs. C: 15.8 ± 4.8, $p = 0.408$) - trabecular bone (%): NS (T: 69.1 ± 18.6 vs. C: 64.7 ± 22.5, $p = 0.183$) *ISQ:* - at implant placement: NS (T: 70.3 ± 5.7 vs. C: 71.7 ± 4.9, $p = 0.679$) - at 6 months: NS (T: 74.4 ± 6.4 vs. C: 75.4 ± 6.4, $p = 0.572$)
Consolo et al. (2007) Institutional	RCT split-mouth 7 months	16	47 ± 5.8 37–57	Bilateral SFE + iliac crest bone graft w/wo PRP	T: PRP *n* = 16 C: no PRP *n* = 16 (No)	4,400 *g*/6 min + thrombin 3:1	*Densitometric values*: SS higher at 4, 5, 6, and 7 months in the PRP group ($p < 0.05$) *Trabecular bone value (%):* SS higher at 4 (T: 43.3 ± 9.1 vs. C: 26.0.3 ± 5.2, $p = 0.048$), 5 (T: 39.3 ± 5.7 vs. C: 29.2 ± 4, $p = 0.046$) and 6 months (T: 29 vs. C: NR, $p = 0.046$). At 7 months: NS (T: 20 vs. C: NR, $p = 0.317$)
Del Fabbro et al. (2015) NR	RCT 10–12 months	30 (30)	52.3 ± 11.6 37–66	SFE + DBBM w/wo PRP	T: DBBM+PRP C: DBBM (Yes)	580 *g*/8 min + CaCl	*Pain (VAS):* SS less pain at 2nd and 3rd day post-surgery in the PRP group (T: NR vs. C: NR, $p < 0.05$) *Quality of life:* SS less swelling, hematoma and discomfort in the PRP group the first 4 days ($p < 0.05$)

(Continues)

TABLE 2 (Continued)

Study (year), funding	Study design, duration	No. of patients (implants)	Mean age ± *SD* and/or range	Surgical procedure	Groups T: test C: control (Smokers included)	PRP preparation	Outcome
Kumar et al. (2015) NR	CCT 12 months	50 (121)	NR 36–69	SFE + mandible AB with PRP or venous blood, implant after 4–6 months post-op	T: PRP *n* = 25 C: Venous blood *n* = 25 (NR)	NR	*Bone height (mm):* SS immediately post-op (T: 18.7 ± 0.2 vs. C: 17.1 ± 0.3, *p* = 0.0002) and at 6 months (T: 17.1 ± 0.2 vs. C: 16.3 ± 0.2, *p* = 0.04). NS at 12 months (T: 17.2 ± 0.3 vs. C: 16.7 ± 0.1, *p* > 0.05) *Implant survival (%):* T: 96.6 vs. C: 100 (*p* = NR)
Schaaf, Streckbein, Lendeckel, Heidinger, Gortz, et al., (2008) NR	RCT 4 months	53	NR	SFE + AB from iliac crest w/wo PRP	T: PRP *n* = 34 C: no PRP *n* = 34 (NR)	1,000 *g*/10 min 2,900 *g*/9 min + 10% calcium gluoconate	*Bone volume (%):* NS (T: NR vs. C: NR, *p* = 0.82)
Schaaf, Streckbein, Lendeckel, Heidinger, Rehmann, et al., (2008) NR	RCT split-mouth 10 months	34 (245)	NR	Bilateral SFE + AB from iliac crest with/without PRP	T: PRP *n* = 34 C: no PRP *n* = 34 (NR)	NR	*Bone density (HU):* NS (T: NR vs. C: NR, *p* = 0.86) *Bone resorption (mm):* NS (T: 0 ± NR vs. C: 2 ± NR, *p* > 0.05) *Implant failure rate:* NS (T: NR vs. C: NR, *p* > 0.05)
Stenport et al. (2011) Institutional	CCT split-mouth 3 months	11	58 35–75	Inlay graft: SFE + AB w/wo PRP onlay graft: iliac bone block with and without PRP	T: PRP *n* = 22 C: no PRP *n* = 22 (NR)	5,600 rpm/15 min 2,400 rpm/10 min + 10% thrombin + CaCl	*Histomorphometry* - new bone/total bone: NS after 3 months in onlay graft (T: NR vs. C: NR, *p* > 0.05) neither inlay graft (T: NR vs. C: NR, *p* > 0.05) - ratio of vessel/total bone: NS in inlay grafts (T: NR vs. C: NR, *p* > 0.05) and in onlay grafts (T: NR vs. C: NR, *p* > 0.05)
Thor et al. (2007) NR	CCT split-mouth 6 months	11	55 36–72	SFE + AB from iliac crest with/without PRP	T: PRP *n* = 11 C: no PRP *n* = 11 (NR)	5,600 rpm/15 min 2,400 rpm/10 min + 10% thrombin + CaCl	*Histomorphometry* - new bone formation (%): SS at 3 months (T: 22 ± 9 vs. C: 11 ± 3, *p* = 0.028) and NS at 6 months (T: 14 ± 7 vs. C: 13 ± 6, *p* > 0.05) - old bone (%): NS at 3 (T: 13 ± 7 C: 20 ± 11, *p* = 0.063) and 6 months (T: 19 ± 10 C: 23 ± 11, *p* > 0.05)

(Continues)

TABLE 2 (Continued)

Study (year), funding	Study design, duration	No. of patients (implants)	Mean age ± *SD* and/or range	Surgical procedure	Groups T: test C: control (Smokers included)	PRP preparation	Outcome
Thor et al. (2005) NR	CCT split-mouth 24 months	19 (152)	58 35–75	inlay graft: SFE + AB from iliac crest w/wo PRP; onlay graft: in the anterior maxilla particulated with PRP and block grafts wo PRP	T: PRP+particulated bone *n* = 19 C: no PRP+block grafts *n* = 19 (Yes)	5,600 rpm/15 min 2,400 rpm/10 min + 10% thrombin + CaCl	*Survival rate (%):* At 1 year (T: 100 vs. C: 97.4, *p* = NR) *Marginal bone level (mm):* NS (T: 1.8 ± 1.1 vs. C: 2.0 ± 0.9, *p* > 0.05) *ISQ:* SS higher values for PRP at abutment connection (T: NR vs. C: NR, *p* < 0.05) and at 1 year follow-up (T: NR vs. C: NR, *p* < 0.05) in the anterior (T: NR vs. C: NR, *p* < 0.05) but not in the posterior maxilla (T: NR vs. C: NR, *p* > 0.05)
Torres et al. (2009) Institutional	RCT split-mouth 24 months	87 (286)	NR 52–78	SFE + DBBM w/wo PRP, followed by implant placement	T: PRP *n* = 74 C: no PRP *n* = 70 (Yes)	60 *g*/6 min + 10% CaCl	*Implant survival (%):* T: 98.6 vs. C: 96.2, *p* = NR *Densitometry (HU):* NS (T: NR vs. C: NR, *p* > 0.05) *Newly formed bone (%):* SS more in PRP group (T: 21.3 ± 4.5 vs. C: NR, *p* < 0.05) *Residual graft volume (%):* NS (T: NR vs. C: NR, *p* > 0.05)
Wiltfang et al. (2003) NR	RCT 6 months	35	T: 45 C: 47 37–54	SFE + β-TCP w/wo PRP, followed by implant placement	T: PRP *n* = 17 C: no PRP *n* = 18 (NR)	NR	*Histology*: - Bone formation (%): SS higher in the PRP group (T: 38 ± NR vs. 29 ± NR, *p* < 0.05) - Degradation of β-TCP (%): NS (T: 13.8 ± NR vs. 15 ± NR, *p* > 0.05)

Note. AB: autologous bone; APC: autologous platelet concentrates; BBG: bovine bone graft (Unilab Surgibone®); CCT: controlled clinical trial; DBBM: deproteinized bovine bone mineral (Bio-Oss®); ISQ: Implant stability quotient; NR: not reported; NS: no statistical difference; RCT: randomized controlled clinical trial; *SD*: standard deviation; SFE: sinus floor elevation; SS: statistical significant difference; β-TCP: tricalcium phosphate; w/wo: with or without; wo: without.

TABLE 3a Included studies: alveolar ridge preservation

Study (year), funding	Study design, duration	No. of patients	Mean age ± *SD* and/or range	Surgical procedure	Groups T: test C: control (smokers included)	PRP preparation	Outcome
Alissa et al. (2010) NR	RCT 3 months	23	30 ± NR 20–52	Tooth extraction with full-thickness flap w/wo PRP	T: PRP *n* = 12 C: no PRP *n* = 11 (Yes)	3,200 rpm/12 min + thrombin 10:1	*VAS:* SS less pain in PRP group at 1st ($p = 0.02$), 2nd ($p = 0.02$) and 3rd ($p = 0.04$) day post-extraction *Soft tissue healing:* SS better in PRP group (T: 4.1 ± 0.6 vs. C: 3.1 ± 1.0, $p = 0.03$) *Radiographic evaluation:* SS denser homogenous trabecular pattern with PRP (62.5% vs. 12.5%, $p = 0.01$) *Bone volume and trabecular architecture*: NS ($p > 0.05$)
Anitua et al. (2015) NR	RCT 10–12 weeks	60	T: 57 C: 53 18–74	Tooth extraction sockets in the mandible w/wo PRGF	T: PRGF *n* = 36 C: no PRGF *n* = 24 (Yes)	580 *g*/8 min + CaCl	*Percentage of regenerated sockets*: SS higher for PRGF (T: 96.7 vs. C: 45.5, $p < 0.001$) *Regenerated volume (%)*: SS higher for PRGF (T: 96.5 ± 8.0 vs. C: 74.6 ± 15.3, $p < 0.001$) *Bone density (HU):* SS higher in PRGF (T: 450 ± 106.7 vs. C: 318 ± 113, $p < 0.001$) *Pain (VAS)*: SS less in PRGF at 3 (T: 0.1 ± 0.5 vs. C: 0.7 ± 0.7 $p < 0.001$) and 7 days (T: 0.0 ± 0.0 vs. C: 0.1 ± 0.3, $p = 0.003$), NS at 15 days (0.0 ± 0.0 vs. 0.0 ± 0.0, $p = 1.0$) *Soft tissue healing score*: SS higher scores in PRGF at 3 (T: 3.9 ± 0.4 vs. C: 2.7 ± 0.7, $p < 0.001$), 7 (T: 4.6 ± 0.5 vs. C: 3.2 ± 0.8, $p < 0.001$) and 15 days (T: 4.9 ± 0.2 vs. C: 3.9 ± 0.6, $p < 0.001$) *Inflammation score*: SS lower score in PRGF at 3 (T: 0.1 ± 0.5 vs. C: 0.8 ± 0.7, $p < 0.001$) and 7 days (T: 0.0 ± 0.0 vs. C: 0.3 ± 0.5, $p < .0001$). NS at 15 days (T: 0.0 ± 0.0 vs. C: 0.0 ± 0.0, $p = 1.0$) *Histomorphometric analysis:* - Percentage of new bone regeneration: SS higher in PRGF (T: 63.1 ± 13.8 vs. C: 35.6 ± 35.3, $p = 0.049$) - Keratinized gingival thickness (μm): SS higher in PRGF (T: 415.4 ± 140.7 vs. C: 274.8 ± 36.0 $p = 0.038$)

(Continues)

TABLE 3a (Continued)

Study (year), funding	Study design, duration	No. of patients	Mean age ± *SD* and/or range	Surgical procedure	Groups T: test C: control (smokers included)	PRP preparation	Outcome
Mozzati et al. (2014) NR	RCT split-mouth 21 days	34	62.7 ± 12.2 NR	Tooth extraction sockets w/wo PRGF in diabetic patients	T: PRGF *n* = 34 C: no PRGF *n* = 34 (Yes)	460 *g*/8 min + CaCl	*Healing Index:* SS better scores in PRGF at 3 days (T: 4.7 ± 1.2 vs. C: 5.4 ± 1.2, $p = 0.01$). NS at 7 days (T: 4.2 ± 0.5 vs. C: 4.7 ± 1.0 $p = 0.09$). SS at 14 days (T: 4.2 ± 0.5 vs. C: 4.6 ± 1.0, $p = 0.02$). NS at 21 days (T: 4.0 ± 0.2 vs. C: 4.1 ± 0.4, $p = 0.33$) *Residual socket volume:* SS smaller in PRGF at 3 (T: 0.20 ± 0.1 vs. C: 0.28 ± 0.1, $p = 0.0007$) and 7 days (T: 0.0 ± 0.0 vs. C: 0.1 ± 0.1 $p = 0.04$). NS at 14 (T: 0.03 ± 0.04 vs. C: 0.06 ± 0.09, $p = 0.1$) and 21 days (T: 0.004 ± 0.01 vs. C: 0.006 ± 0.016, $p = 0.12$) *Bone density (HU):* SS higher in PRGF (T: 450 ± 106.7 vs. C: 318 ± 113, $p < 0.001$) *Pain (VAS)*: SS less in PRGF at 3 (T: 0.1 ± 0.5 vs. C: 0.7 ± 0.7 $p < 0.001$) and 7 days (T: 0.0 ± 0.0 vs. C: 0.1 ± 0.3, $p = 0.003$), NS at 15 days (0.0 ± 0.0 vs. 0.0 ± 0.0, $p = 1.0$)
Farina et al. (2013) Institutional	CCT 10 weeks	28	T: 57 C: 52.5 34–74	Extraction sockets w/wo PRGF	T: PRGF *n* = 11 C: no PRGF *n* = 17 (Yes)	580 *g*/8 min + CaCl	*Micro-CT:* - Bone volume (mm3): NS at 4 (T: 1.4 ± 2.0 vs. C: 3.1 ± 3.4, $p = 0.177$) and 8 weeks (T: 3.2 ± 2.9 vs. 4.5 ± 2.7, $p = 0.792$) - Tissue mineral content (mg): NS at 4 (T: 0.7 ± 1.0 vs. C: 1.8 ± 2.0, $p = 0.177$) and 8 weeks (T: 1.7 ± 1.8 vs. C: 2.5 ± 1.7, $p = 0.662$) - Tissue mineral density (mg/cm3): NS at 4 (T: 480 ± 97.6 vs. C: 519.4 ± 123.5, $p = 0.329$) and 8 weeks (T: 485.8 ± 73.0 vs. C: 538.4 ± 106.0, $p = 0.429$) *Histology:* - Mean number of CD68 + cells: NS ($p > 0.05$) - Mean number of vVW+cells: NS ($p > 0.05$) - Mean OCN staining: NS ($p > 0.05$)

TABLE 3b Included studies: alveolar ridge augmentation

Study (year), funding	Study design, duration	No. of patients	Mean age ± *SD* and/or range	Surgical procedure	Groups T: test C: control (smokers included)	PRP preparation	Outcome
Eskan et al. (2014) Industry	RCT 4 months	32	NR 19–75	Ridge augmentation with cancellous allograft w/wo PRP + SM	T: PRP *n* = 14 C: no PRP *n* = 14 (No)	NR + thrombin + 10% CaCl	*Ridge width at crest (mm):* SS better in PRP group (T: 2.9 ± 1.0 vs. C: 2.0 ± 1.2, $p < 0.05$) *Ridge width 5 mm apical to crest (mm):* NS (T: 7.9 ± 1.7 vs. C: 7.5 ± 0.9, $p > 0.05$) *Loss of augmented ridge (mm):* NS (T: 2.4 ± 1.6 vs. C: 2.8 ± 1.4, $p > 0.05$) *Alveolar ridge height changes (mm):* NS between the groups ($p > 0.05$) *Histology:* - Vital bone (%): SS more in the PRP group (T: 51 ± 15 vs. C: 36 ± 14, $p < 0.05$) - Trabecular space (%): NS (T: 42 ± 15 vs. C: 54 ± 13, $p > 0.05$)
Torres et al. (2010) Institutional	RCT 30 months	30	NR 48–76	Ridge augmentation + DBBM + Ti-mesh w/wo PRP, followed by implant placement after 6 months	T: PRP *n* = 15 C: no PRP *n* = 15 (Yes)	160 *g*/6 min + 10% CaCl	*Average bone height (mm):* SS more gain in PRP group (T: 3.5 ± 0.7 vs. C: 3.1 ± 0.8, $p < 0.05$) *Average bone width (mm):* SS more gain in PRP group T: 4.1 ± 0.6 vs. C: 3.7 ± 0.6, $p < 0.05$) *Mesh exposure (%):* SS more exposure in the control group (T: 0 vs. C: 28.5, $p < 0.05$) *Survival rate (%):* NS (T: 100 vs. C: 97.3, $p > 0.05$)

Note. CaCl: calcium chloride; CCT: controlled clinical trial; DBBM: deproteinized bovine bone mineral (Bio-Oss®); HU: hounsfield unit; NR: not reported; cancellous allograft (RegenerOss®); NS: no statistical difference; PRGF: plasma rich in growth factors; RCT: randomized controlled clinical trial; *SD*: standard deviation; SS: statistical significant difference; SM: synthetic membrane; Ti-mesh: titanium mesh; VAS: visual analogue scale; w/wo: with or without; wo: without.

TABLE 4 Included studies: dental implants

Study (year), funding	Study design, duration	No. of patients (implants)	Mean age ± *SD* and/or range	Surgical procedure	Groups T: test C: control (Smokers included)	PRP preparation	Outcome
ArRejale et al. (2016) Institutional	RCT split-mouth 12 months	16 (32)	NR NR	DBBM + CM w/wo PRP in defects of immediate implants in the maxillary anterior or premolar region	T: DBBM + PRP *n* = 16 C: DBBM wo PRP *n* = 16 (No)	200 *g*/20 min 400 *g*/10 min	*Horizontal depth of the defect (mm):* SS lower in the PRP group at 12 months at 2 mm (T: 3.0 ± 0.0 vs. C: 2.0 ± 0.0, $p = 0.01$) and 6 mm (T: 4.5 ± 0.0 vs. C: 3.6 ± 0.0, $p = 0.01$) apical from the crest *Horizontal bone width (mm):* SS more width in the PRP group at 12 months at 2 mm (T: 3.5 ± 0.1 vs. C: 2.8 ± 0.2, $p = 0.04$) and 6 mm (T: 4.9 ± 0.1 vs. C: 4.0 ± 0.2, $p = 0.04$) apical to the crest. NS at the crest (T: 1.7 ± 0.2 vs. C: 1.4 ± 0.2, $p = 0.51$) and at the end of the implant (T: 4.8 ± 0.4 vs. C: 4.5 ± 0.4, $p = 0.53$) *Bone density:* SS higher density in the PRP group at 9 (T: 128.9 ± 3.6 vs. C: 108.1 ± 4.8, $p = 0.13$) and 12 months (T: 129.3 ± 3.2 vs. C: 106.4 ± 3.1, $p = 0.0008$). NS at 3 (T: 130.3 ± 3.2 vs. C: 123.8 ± 4.3, $p = 0.54$) and 6 months (T: 132 ± 3.6 vs. C: 120.5 ± 4.4, $p = 0.20$) *Mean marginal bone loss (mm):* SS less bone loss in PRP group at 6 (mesial; T: 1.3 ± 0.2 vs. C: 2.7 ± 0.3, distal; 1.4 ± 0.2 vs. 2.5 ± 0.3, $p = 0.001$), 9 (mesial; T: 0.8 ± 0.2 vs. C: 1.6 ± 0.2, distal; 0.8 ± 0.2 vs. 1.6 ± 0.2, $p = 0.0001$) and 12 months (mesial; T: 0.8 ± 0.2 vs. C: 1.6 ± 0.2, distal; 0.8 ± 0.7 vs. 1.5 ± 1.0, $p < 0.001$). NS at 3 months (mesial; T: 1.6 ± 0.2 vs. C: 2.2 ± 0.4, distal; 1.7 ± 0.2 vs. 2.1 ± 0.4, $p = 0.67$)
Georgakopoulos et al. (2014) NR	RCT 8 months	30 (76)	NR 25–65	Implant placement w/wo PRP	T: PRP *n* = 15 C: wo PRP *n* = 16 (No)	2,400 rpm/10 min 3,600 rpm/15 min + 10% CaCl	*ROC analysis of panoramic radiographs (AUC):* PRP has a positive effect - Angular second moment: (T: 0.80 vs. C: 0.66, p = NR) - Correlation: (T: 0.78 vs. C: 0.61, p = NR) - Long run emphasis: (T: 0.77 vs. 0.56, p = NR) - Gray level non uniformity: (T: 0.81 vs. 0.68, p = NR)
Kundu & Rathee (2014) Self-funded	RCT 3 months	NR (30)	33.9 ± 11.2 18–56	One-stage implants coated w/wo PRP and loaded within 2 weeks	T1: PRP squared thread *n* = NR T2: PRP reverse buttress thread form *n* = NR C1: non PRP squared thread *n* = NR C2: non PRP reverse buttress thread form *n* = NR (No)	2,400 rpm/10 min 3,600 rpm/15 min	*Implant stability (Periotest):* SS only at baseline between PRP and no PRP (T: 1.0 ± 6.6 vs. C:-4.4 ± 2.2, $p = 0.003$). NS at 1 and 3 months ($p > 0.05$) *Changes of bone height:* NS at baseline, 1 and 3 months ($p > 0.05$)
Monov et al. (2005) NR	CCT split-mouth 44 days	10 (34)	67 53–80	One-stage implants in the mandible w/wo PRP	T: PRP (left side) *n* = 10 C: wo PRP (right side) *n* = 10 (NR)	2,400 rpm/10 min 3,600 rpm/10 min	*Implant stability (RFA):* NS (T: 6,167–6,363 vs. C: 6,103–6,230, $p > 0.05$)

Note. AUC: area under the curve; CaCl: Calcium chloride; CM: collagen membrane; CCT: controlled clinical trial; DBBM: deproteinized bovine bone mineral(Bio-Oss®); NR: not reported; NS: no statistical difference; ROC: receiver operating characteristic; RFA: resonance frequency analysis; RCT: randomized controlled clinical trial; *SD*: standard deviation; SS: statistical significant difference; w/wo: with or without; wo: without.

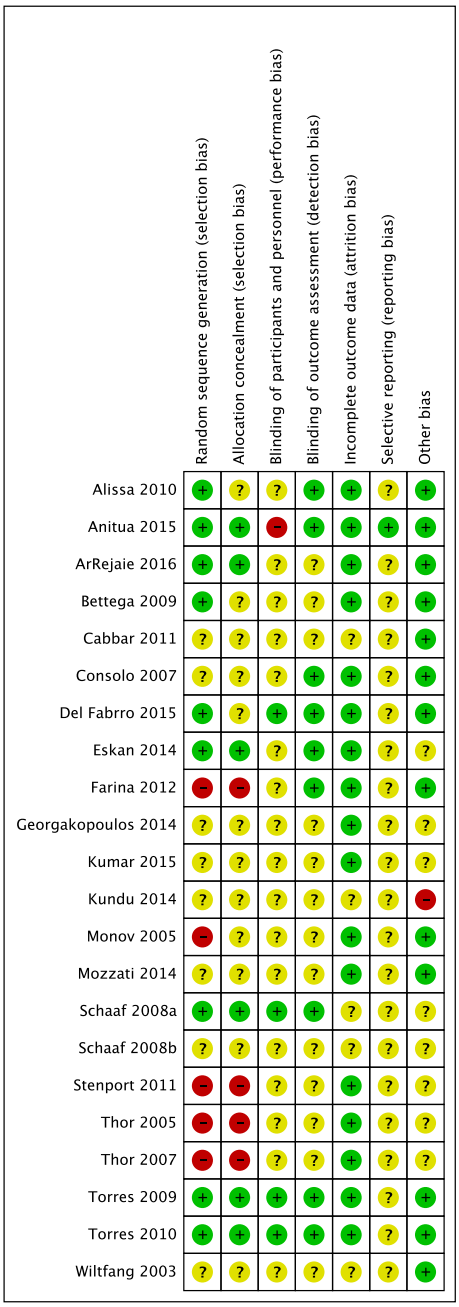

FIGURE 2 Quality assessment of the included studies: Risk of bias summary

reduced mesh exposure (Torres et al., 2010). Survival rates were similar for both groups (Torres et al., 2010), along with greater apical ridge width and alveolar height changes (Eskan et al., 2014) (Table 3b).

3.10 | Implant placement (56 patients in three studies and one study that did not report the number of patients)

Four studies used PRP during implant placement. Only one study performed GBR (ArRejaie et al., 2016). PRP enhancing bone formation was found in two studies (ArRejaie et al., 2016; Georgakopoulos et al., 2014). This was associated with larger bone width, higher bone density and less marginal bone loss (ArRejaie et al., 2016; Georgakopoulos et al., 2014). When looking at implant stability, data are scarce (from 40 patients) and pointing toward no differences (Kundu & Rathee, 2014; Monov et al., 2005) (Table 4).

4 | DISCUSSION

The present systematic review focused on RCT and CCT studies using PRP in all fields connected to implant dentistry including sinus floor augmentation, socket preservation, ridge augmentation or peri-implantitis. The aim was to evaluate the current knowledge with respect to the clinical indications of PRP on soft tissue healing and bone regeneration with respect to implant placement. Analysis of the selected publications revealed heterogeneity of results with a general lack of conclusive evidence, mainly because of being underpowered, and incomplete reporting of study design. Owing to the heterogeneity of the study design, the various outcome measures, and the slightly different method of preparing PRP, no meta-analysis could be performed—neither for bone formation and soft tissue healing nor for implant stability, osseointegration, and implant survival.

4.1 | Sinus floor elevation

A previous systematic review suggested that PRP might improve SFE outcome parameters (Bae, Kim, & Myung, 2011). The present report is based on 12 clinical trials when grafting materials were combined with PRP. Results are conflicting. PRP increased bone formation and bone height in four studies (Kumar et al., 2015; Thor et al., 2007; Torres et al., 2009; Wiltfang et al., 2003). These positive findings, however, should be interpreted with caution. For example, Kumar et al. described a greater bone height in the PRP group immediately after surgery but this difference disappeared at the 12-month follow-up. The positive outcome in favor of PRP up to 6 months could be explained by the surgical procedure per se rather than the use of PRP. Torres et al. reported more bone formation in the PRP group, however, the histological analysis included biopsies from only five patients and not from the whole sample. All other parameters, including implant survival and densitometry, were not significant. Similarly, Thor et al. described higher bone formation in the PRP group at the 3-month follow-up, nonetheless, these differences disappeared after 6 months.

In line with these findings, other studies failed to find significant differences when using a variety of bone graft materials (autologous bone from the iliac crest, DBBM, BBG, β-TCP), different surgical approaches and variable residual bone heights before the intervention. In the majority of studies, residual graft size and graft resorption were found to be similar among the groups as well as implant survival rates (Cabbar et al., 2011; Kumar et al., 2015; Schaaf, Streckbein, Lendeckel, Heidinger, Rehmann, et al., 2008; Thor et al., 2005; Torres et al., 2009).

Another aspect that was evaluated in two studies was implant stability measured by ISQ values (Cabbar et al., 2011; Thor et al., 2005). While Cabbar et al. found no significant differences, Thor

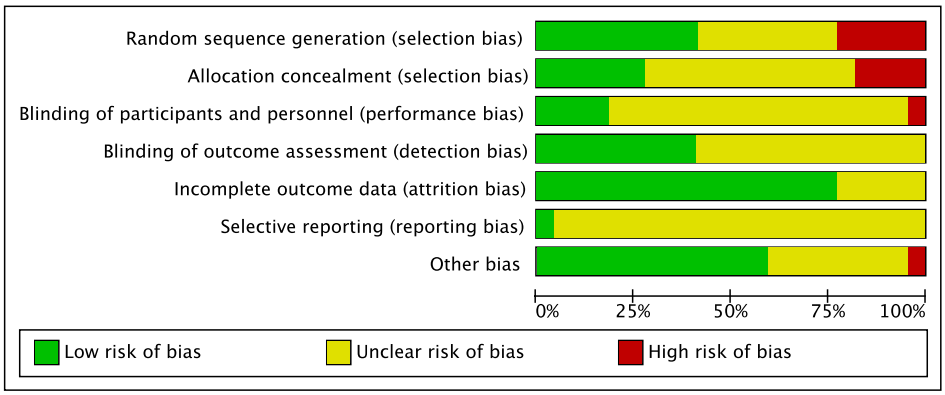

FIGURE 3 Quality assessment of the included studies: Risk of bias graph

et al. reported higher ISQ values at abutment connection in the PRP group. The latter study performed inlay grafts for SFE and onlay grafts for the anterior maxilla followed by implant placement. At 1-year follow-up, however, significant differences were detected only in the anterior maxilla (Thor et al., 2005). This should be interpreted with prudence, as it is questionable if this statistical difference suggests a clinical benefit of PRP. Furthermore, there is a lack of data based on the long-term outcomes by means of PRP.

In summary, inconclusive results are reported because of underpowered studies lacking hard endpoints. None of the studies included used PRP without a grafting material. Therefore, the effect of PRP alone on bone regeneration during SFE remains questionable.

4.2 | PRP and alveolar bone regeneration

Based on the growth factors contained in PRP, filling a post-extraction socket with PRP has the potential to improve bone regeneration and soft tissue healing. The ultimate goal is to enhance wound healing and facilitate implant placement in a prosthetically driven position. It should be pointed out that the included studies applied PRP or PRGF. Even though both preparations showed beneficial results, caution should be taken when drawing a conclusion, as for PRP in extraction sockets only one study with a small patient number could be included, and for PRGF heterogenous results have been stated. PRGF differs from PRP in that it is depleted of leukocytes.

Two studies (Anitua et al., 2015; Farina et al., 2013) reported on bone regeneration at extraction sockets using PRGF. In one study (Anitua et al., 2015) the use of PRGF enhanced bone regeneration defined as the percentage of patients with a regenerated socket ≥75% at 10–12 weeks. Histomorphometric analysis confirmed the greater bone regeneration with PRGF. Farina et al., on the other hand, when using PRGF were unable to reproduce these positive outcomes in terms of bone volume. This inconsistency may be due to the small sample size and shorter follow-up in one of the studies and different number or application of membranes and clots (Farina et al., 2013). While Anitua et al. included 36 patients in the test group, Farina et al. included only 11 patients put into two different time points. Anitua et al. performed the analysis after 10–12 weeks whereas Farina et al. conducted the analysis after 4–8 weeks. Further studies are required to establish the benefit of PRGF and PRP for this clinical indication.

Three studies (Alissa et al., 2010; Anitua et al., 2015; Mozzati et al., 2014) reported outcomes using a soft tissue healing index. PRP improved wound and soft tissue healing during the first 15 days. An interesting approach was carried out by Mozzatti et al. in insulin-dependent patients. The use of PRGF improved the wound healing during the first 2 weeks. In this context, PRGF might be an attractive approach in systemically compromised patients to achieve rapid wound healing. Nevertheless, the clinical interpretation is difficult due to the plethora of healing indexes not commonly used.

Two of the aforementioned studies (Alissa et al., 2010; Anitua et al., 2015) further provided positive outcomes of bone density measured by radiographs and cone beam computer tomography at 3 months. However, bone density is not a suitable outcome for alveolar ridge preservation or at least it is difficult to interpret from a clinical point of view. Thus, there is great necessity for appropriately designed studies to further evaluate dimensional changes utilizing PRP in various clinical situations considering medically compromised patients.

Two studies reported on alveolar ridge augmentation procedures with PRP (Eskan et al., 2014; Torres et al., 2010) detecting beneficial results such as increased crestal ridge width, a higher percentage of vital bone, higher gain of bone height and width and less mesh exposure. Eskan et al. showed a significant higher value for ridge width at the crest in the test group, but they did not provide detailed information about the initial bone volume deficiency. Torres et al. showed gain of bone height and width, however, the additional bone gain in the PRP group was only about 0.4 mm. Patients enrolled had insufficient bone height of up to 7 mm and/or bone width of up to 3 mm. The lack of detailed data in both studies precludes a comprehensive comparison of the results. One noteworthy finding, however, was the absence of titanium mesh exposure in the PRP group compared to 28.5% in the control group (Torres et al., 2010). Overall, given the low number of studies and the different surgical approaches used, it is difficult to generate clinical recommendations.

4.3 | PRP and pain

Pain is an important patient-reported outcome measure and significantly determines the quality of patient's oral surgery experience (Coulthard, Patel, Bailey, & Armstrong, 2014). Three studies included patient-reported outcome measures, mainly using the Visual Analogue Scale. However, the positive effect of PRP on postoperative pain was considered biased in two of three studies due to lack of blinding. All outcomes can be affected by lack of blinding as there is a special risk of bias with subjective outcomes such as pain (Wood et al., 2008). Consequently, the present data must be interpreted with caution. Significantly less pain was reported in the PRP group for SFE (Del Fabbro et al., 2015) and for alveolar ridge preservation (Alissa et al., 2010; Anitua et al., 2015). Del Fabbro et al. showed a significant difference in SFE only after 2 and 3 days. From the 4th day on, the significant difference disappeared, which is in line with the results from Alissa et al. who detected differences between the groups only until the 3rd day post-op while Anitua et al. observed less pain during the first 7 days in the PRGF group. In summary, owing to study design there is not enough evidence to support that PRP reduces pain after the surgical procedure.

Another aspect that should be considered is the postoperative swelling. Only one study assessed swelling after sinus lift elevation (Del Fabbro et al., 2015). Patients in the PRP group perceived less swelling during the first 4 days postoperatively. However, this parameter was measured using a self-administered questionnaire. As a result, more studies are warranted.

4.4 | Dental implants

With respect to PRP application during implant placement, only three RCTs and 1 CCT were included. Two studies assessed implant stability at different time-points with inconsistent results (Kundu & Rathee, 2014; Monov et al., 2005). Only one study found significant higher ISQ values in the PRP group at implant placement (Kundu & Rathee, 2014) that were no longer present after 1 and 3 months. PRP was found to provide a higher bone width, higher bone density, and less marginal bone resorption at 9 and 12 months (ArRejaie et al., 2016). Despite these positive findings, it remains unclear if PRP predictably improves osseointegration, implant success and survival.

4.5 | Peri-implantitis

Regarding the application of PRP during peri-implantitis treatment, no RCT or CCT could be found in the present systematic review. Thus, it remains unknown what effect PRP may play in the treatment of peri-implantitis, precluding any clinical recommendation.

5 | CONCLUSION

On the basis of studies with limited statistical power, the present review demonstrated that (i) for SFE PRP/PRGF combined with grafting materials may transiently enhance bone formation, (ii) for alveolar ridge preservation PRP/PRGF might improve bone regeneration and wound healing, (iii) PRP might reduce postoperative pain and swelling, and finally (iv) for implant placement and peri-implantitis defects there is a lack of adequate studies on PRP.

6 | FUTURE DIRECTION

The studies included in the present review mainly focused on surrogate parameters to evaluate the effect of PRP. The clinical relevance of the outcome measurements remains questionable. A low number of studies were found to be included for PRP during implant placement and ridge augmentation. An interesting aspect that requires further attention is to investigate what effects PRP might bring under demanding clinical situation, for example in medically compromised patients or in extraction sockets with severe buccal bone deficiency. One area of research that needs to be determined is for which clinical settings PRP should be used alone or in combination with grafting materials. In order to provide the clinicians with data or even guidelines whether to use PRP or not, in which clinical situations and for what kind of patients further well-designed RCTs are warranted.

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CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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